



caBIGTM
cancer Biomedical
Informatics Grid™

A nanoparticle ontology for cancer research

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*Washington University in St. Louis
Center for Computational Biology*



Talk overview



Talk overview



- **Overview of vocabulary for cancer nanotechnology research**
 - Cancer nanotechnology needs
 - Vocabulary overview
 - Ontology development at Wash U/SCCNE
 - Ontology applications

Talk overview



- **Overview of vocabulary for cancer nanotechnology research**
 - Cancer nanotechnology needs
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 - Ontology development at Wash U/SCCNE
 - Ontology applications
- **Ontology development challenges and needs**
 - Community development
 - Mappings and harmonization
 - User interaction

Cancer nanotechnology needs



- In Vitro Studies
- In Vivo Animal Model Studies
- Nanoparticle Preparation and Characterization Studies
- Clinical Trials



NANOPARTICLE DATA

- Chemical composition
- Physical property
- Characterization
- Preparation
- Stability to pH, temperature, light, magnetic field, ultrasound
- Others

TUMOR VASCULATURE, IN VIVO ANIMAL MODEL DATA

- Tumor size/volume
- Blood vasculature
- Tumor cell density
- Endothelial gap size
- pH vs. distance from vessel wall
- pO₂ vs distance from vessel wall
- Molecular expression levels (e.g. VEGF, bFGF, bradykinin level, etc.)
- Interstitial fluid pressure
- Tumor blood flow (velocity, viscosity, arterial pressure, venous pressure)
- Animal models

EFFICACY DATA FOR APPLICATION

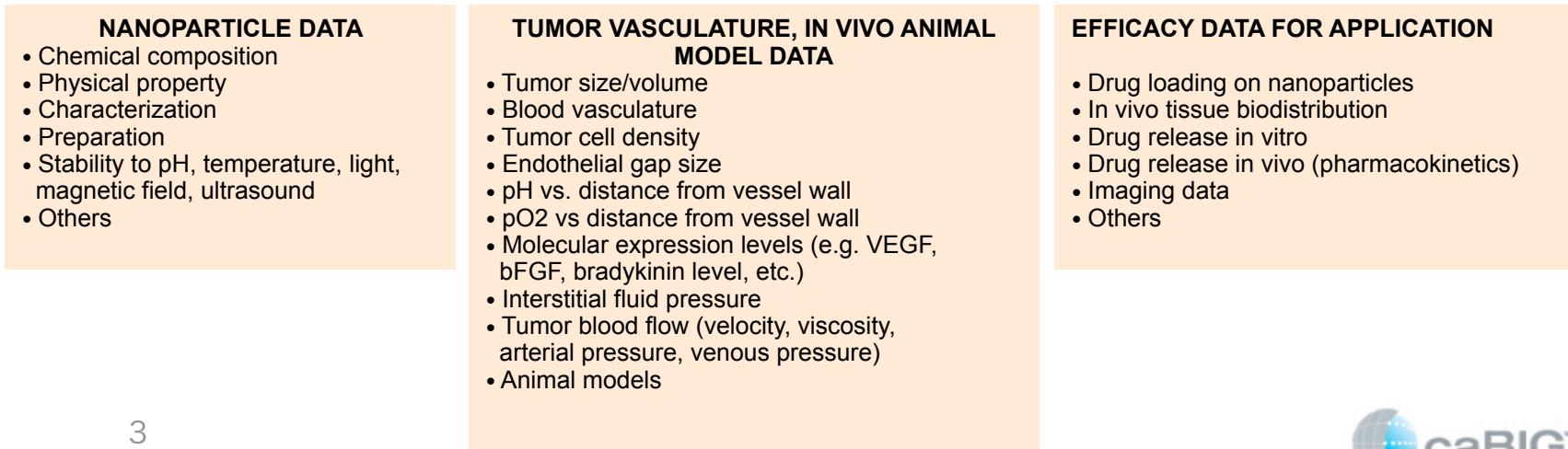
- Drug loading on nanoparticles
- In vivo tissue biodistribution
- Drug release in vitro
- Drug release in vivo (pharmacokinetics)
- Imaging data
- Others

Cancer nanotechnology needs



- **Cancer nanotechnology data is:**
 - Diverse but detailed: specialized data of various types
 - Multidisciplinary: scattered across literature and databases, terms from various fields

- In Vitro Studies
- In Vivo Animal Model Studies
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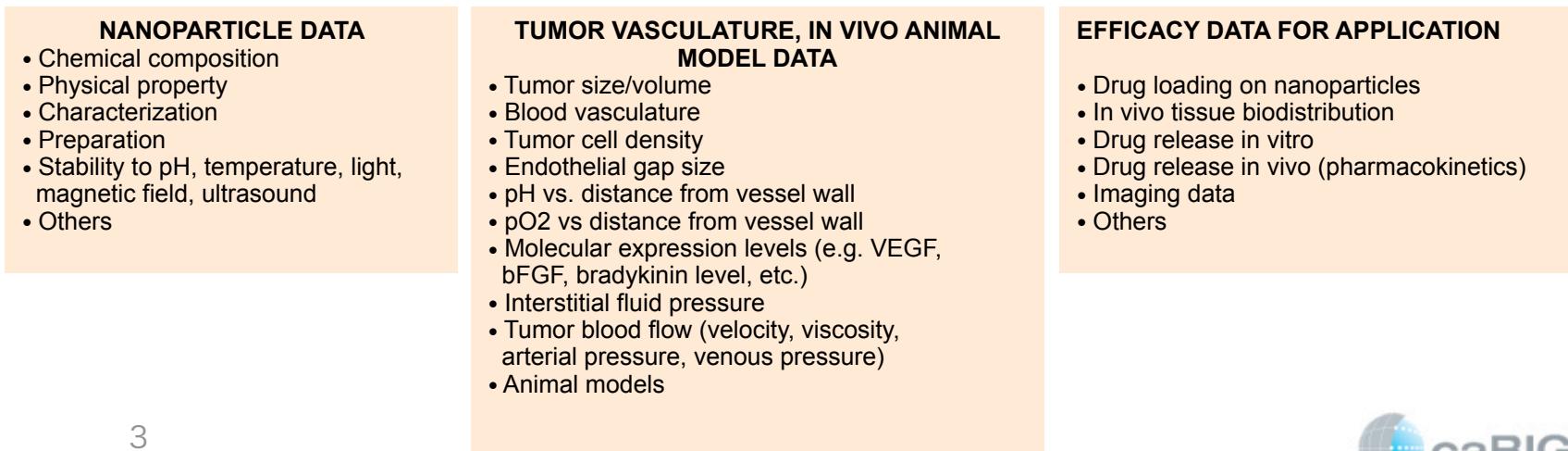


Cancer nanotechnology needs



- **Cancer nanotechnology data is:**
 - Diverse but detailed: specialized data of various types
 - Multidisciplinary: scattered across literature and databases, terms from various fields
- **Need informatics resources to provide useful tools to researchers:**
 - Databases
 - Common vocabularies

- In Vitro Studies
- In Vivo Animal Model Studies
- Nanoparticle Preparation and Characterization Studies
- Clinical Trials



Data diversity



Source: Son et al, J. Controlled Release, 51, 135-145 (2003)

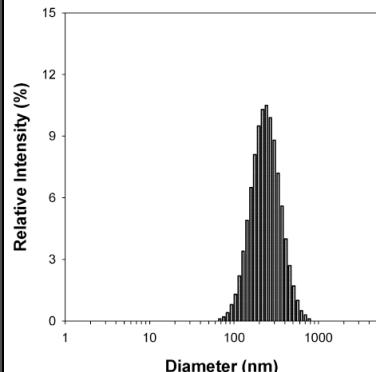
Data diversity

Chemical composition

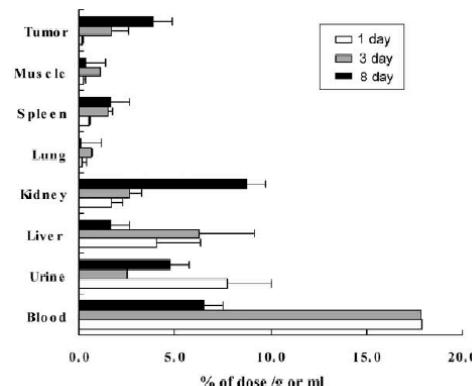
Preparation



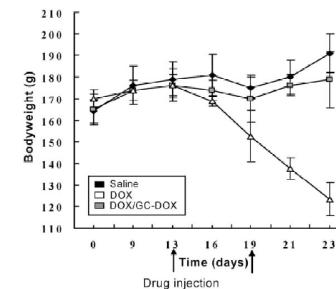
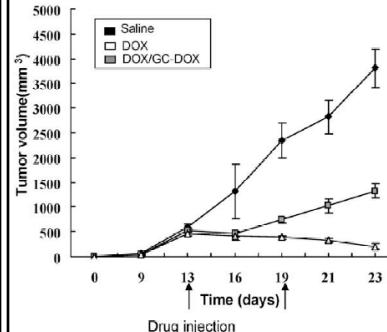
Size distribution data



Tissue biodistribution



Anti-tumor activity



Zeta Potential

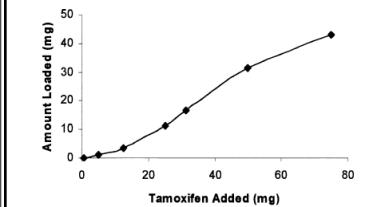
Table 1
Zeta potential values of control and tamoxifen loaded nanoparticles^a

Nanoparticle formulations	Zeta potential (mV)
Control nanoparticles	6.7 ± 1.2 ^b
Tamoxifen-loaded nanoparticles	25.4 ± 1.4

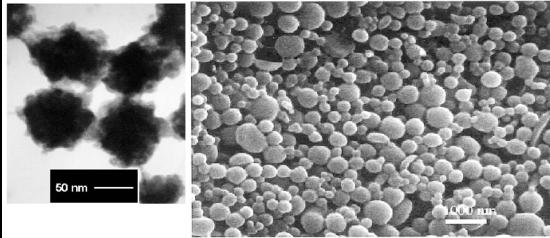
^a Zeta potentials of the nanoparticle suspension in deionized distilled water were measured using the Brookhaven's Zeta PALS instrument.

^b Mean ± S.D. ($n = 8$).

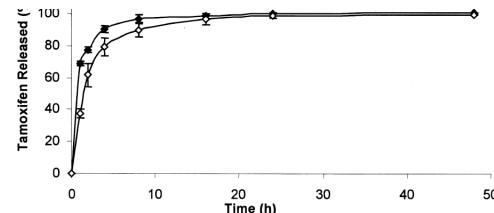
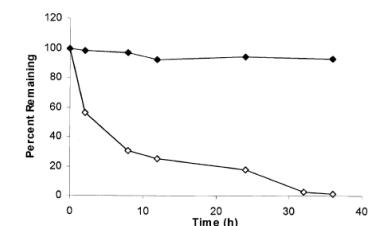
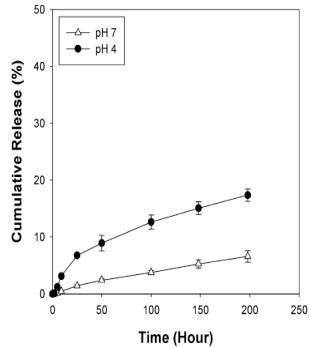
Drug loading data



Surface morphology data

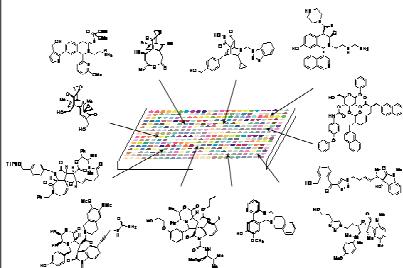


In vitro drug release



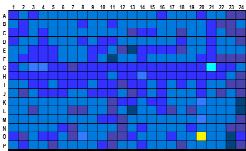
Source: Son et al, J. Controlled Release, 51, 135-145 (2003)

Data diversity



Nanoparticles (n=51)

- 0.01, 0.03, 0.1, 0.3 mg/ml Fe
- core composition
- surface modification
- experimental probes
- commercially available
- human use



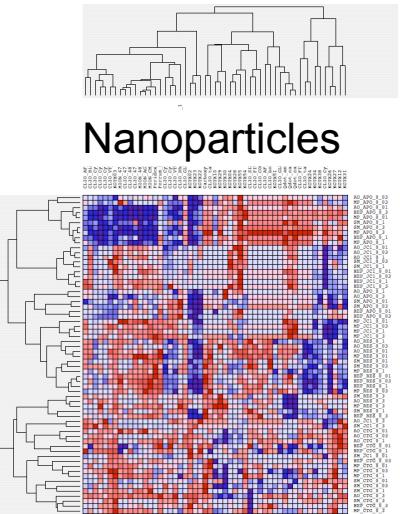
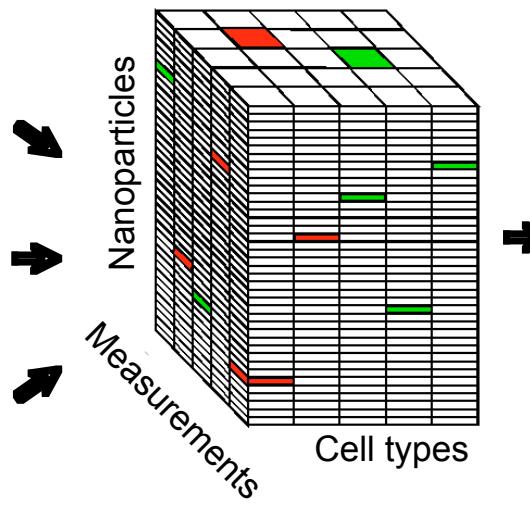
Metabolic measurement

- apoptosis
- atp content
- reducing potential
- mitochondrial potential



Cell types

- endothelial
- hepatic
- macrophage
- vascular smooth muscle



Analyze
profiles

Stanley Shaw and Ralph Weissleder, NHLBI TPEN at MGH

Source: Shaw SY et al, Proc Natl Acad Sci USA, 105, 7387 (2008).

Cancer nanotechnology vocabularies

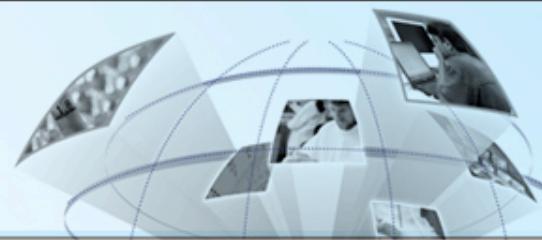


Cancer nanotechnology vocabularies



- One piece of the “nanoinformatics” puzzle

Cancer nanotechnology vocabularies



- **One piece of the “nanoinformatics” puzzle**
- **Goal:**
 - Help integrate and standardize data across disciplines
 - Provide user access to search, browse, etc.
 - Inference and design

Cancer nanotechnology vocabularies



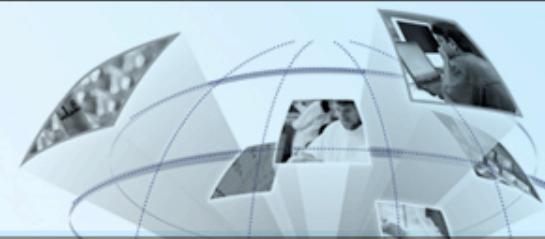
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 - Large vocabulary projects have many needed ingredients:
 - NCI Metathesaurus/EVS
 - BiomedGT SMW

Cancer nanotechnology vocabularies



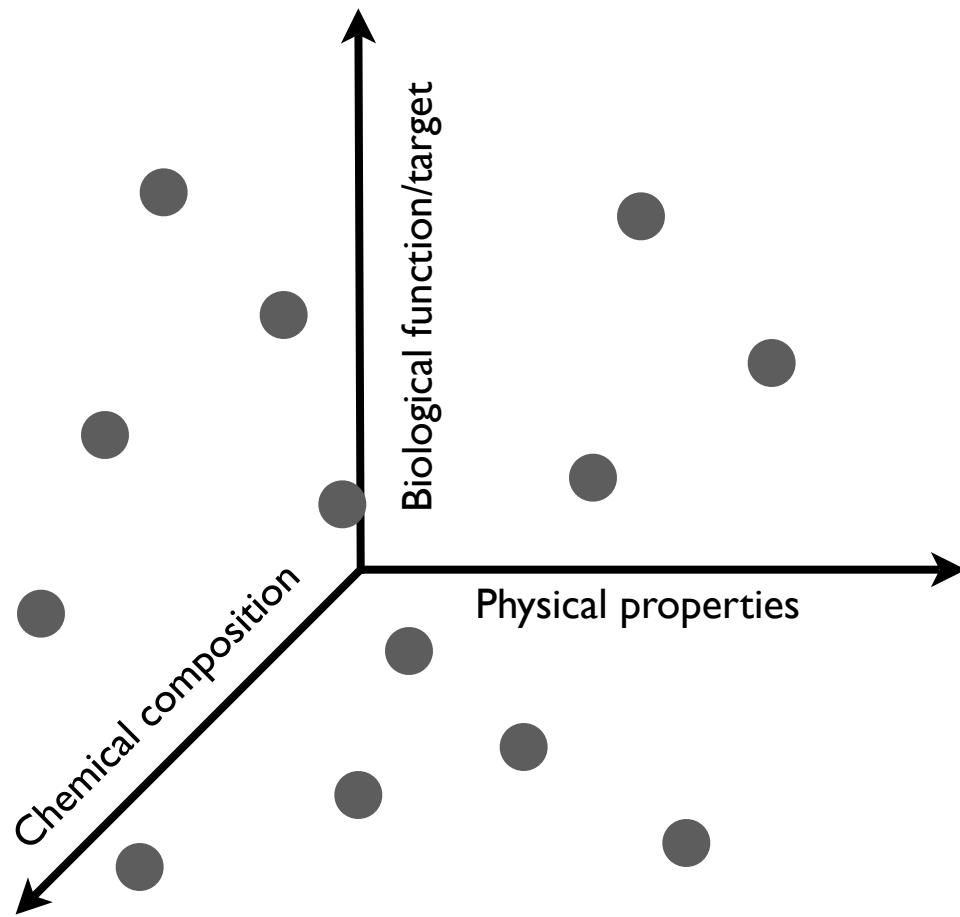
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 - Specialized vocabulary projects have important elements:
 - Stanford and Georgia Tech project-specific ontologies
 - ChEBI, GO, SNOMED_CT for domain-specific terms

Cancer nanotechnology vocabularies

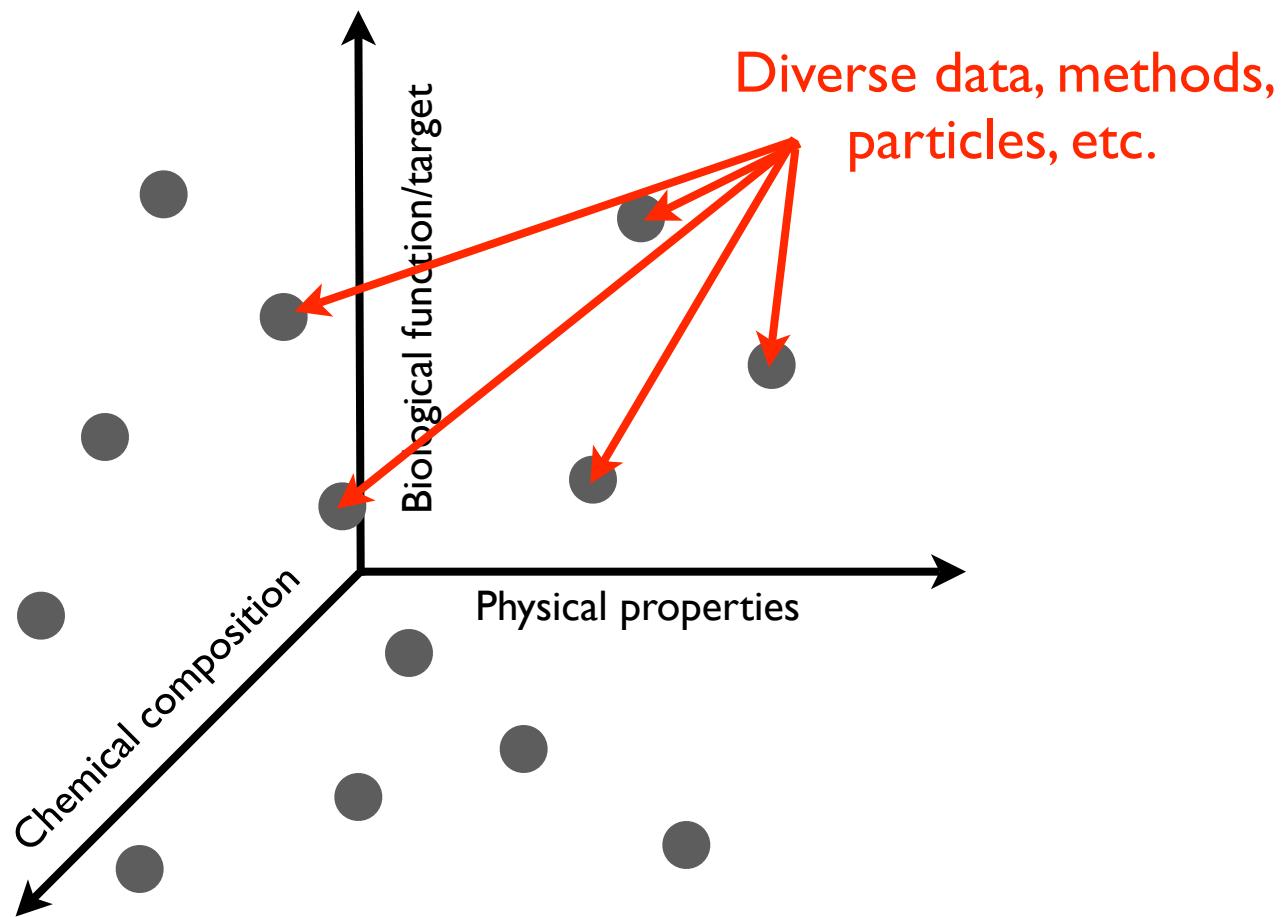


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 - Specialized vocabulary projects have important elements:
 - Stanford and Georgia Tech project-specific ontologies
 - ChEBI, GO, SNOMED_CT for domain-specific terms
 - Integrated ontology for cancer nanotechnology research:
 - Describe terminology and relationships unique to nanotechnology
 - Describe applications to cancer
 - Integrate (and cross-reference!) other vocabularies for multi-disciplinary concepts
 - Wash U/SCCNE NanoParticle Ontology (NPO)

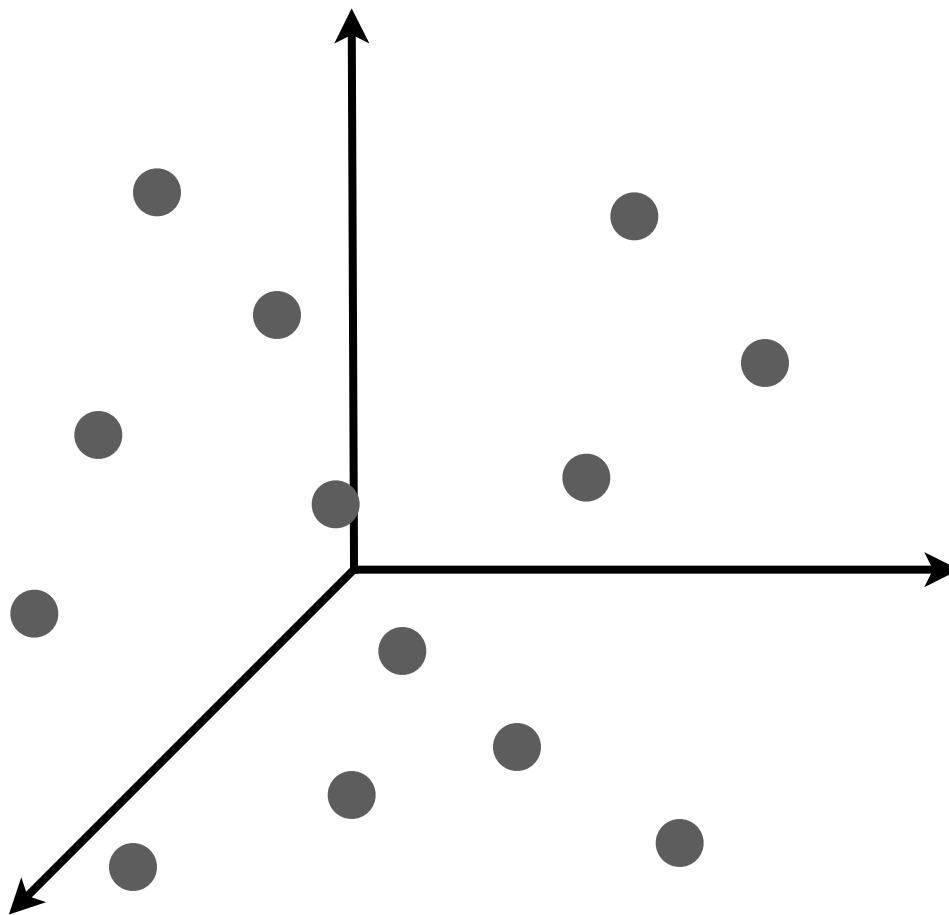
Our view of nanoinformatics



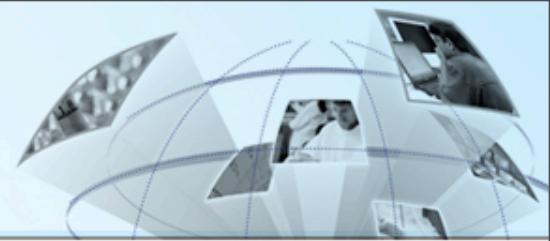
Our view of nanoinformatics



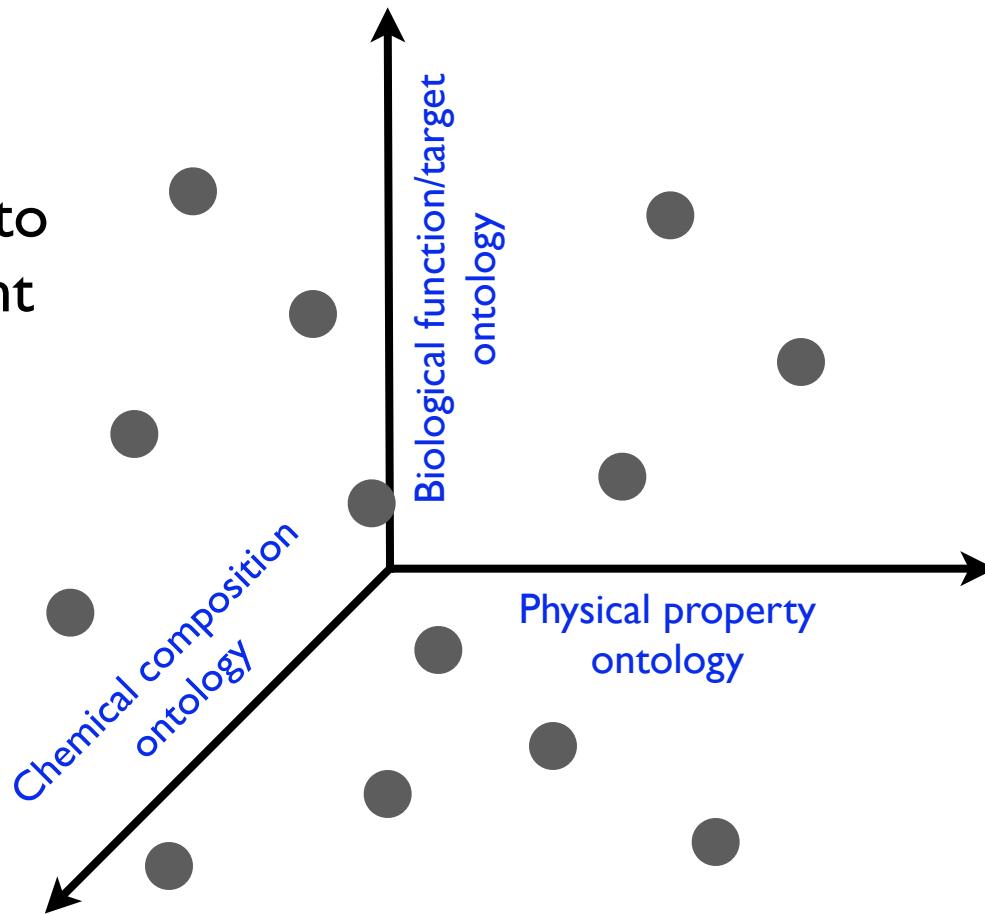
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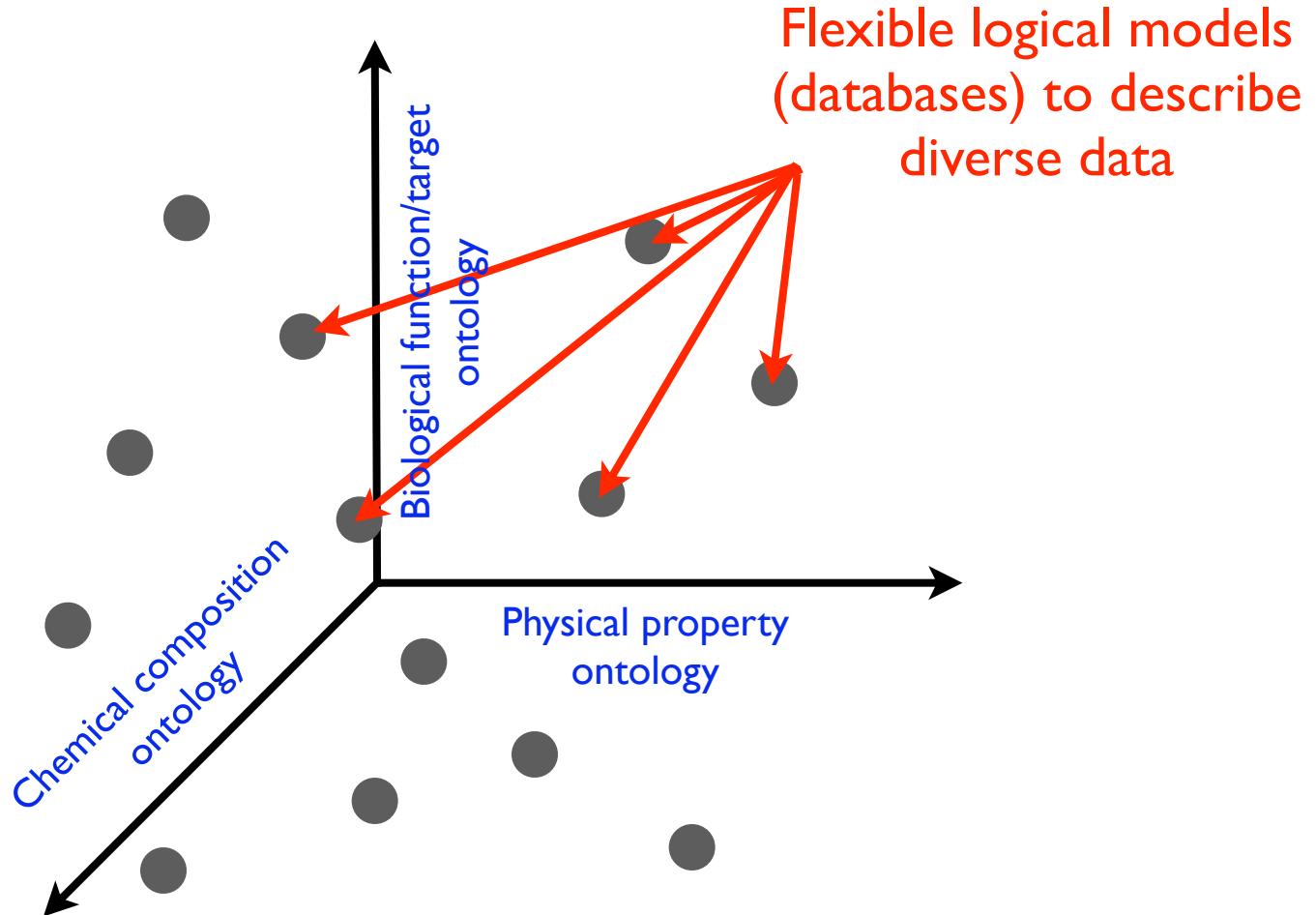
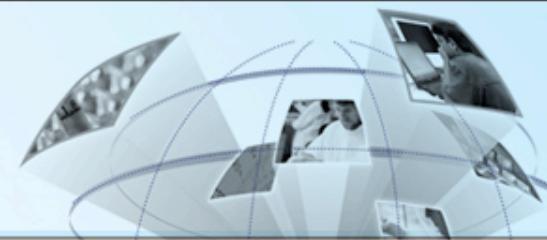
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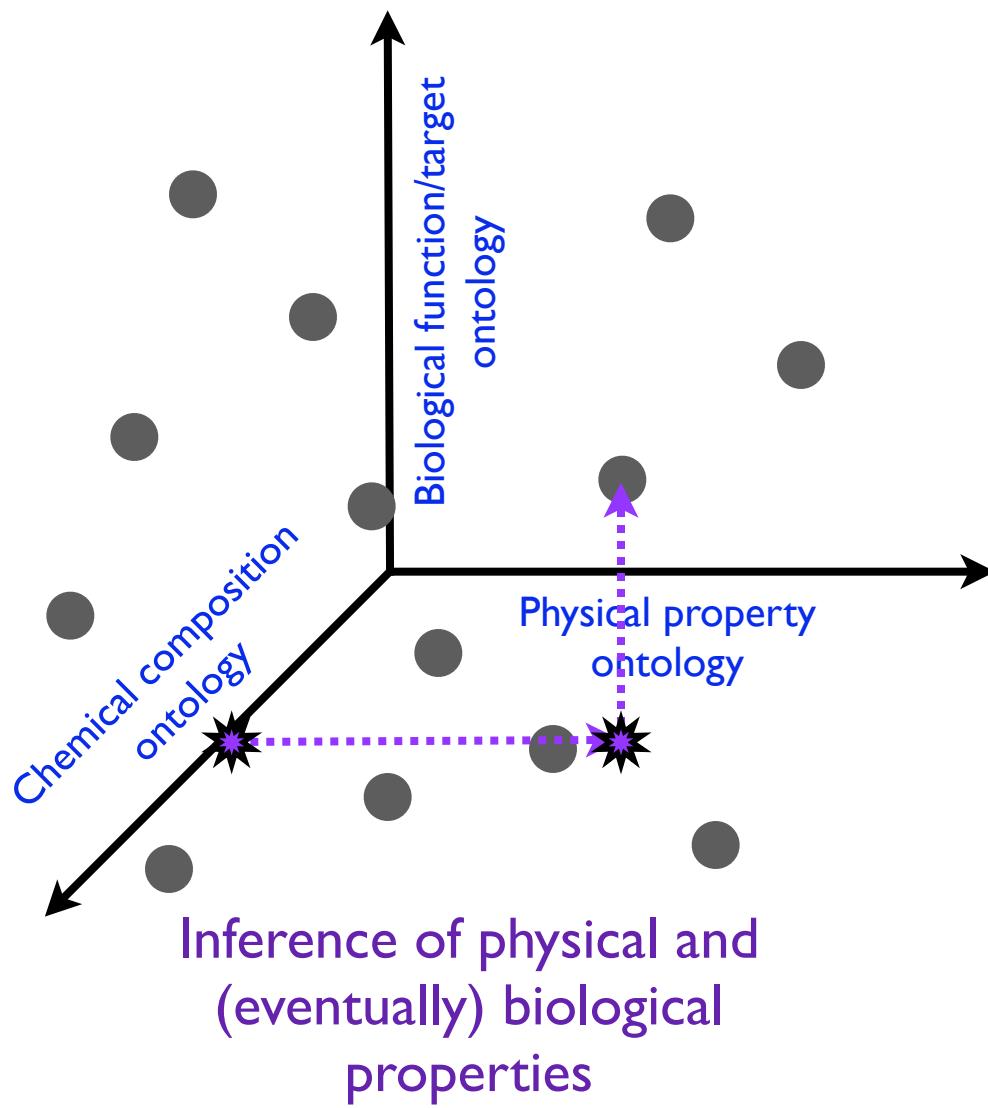
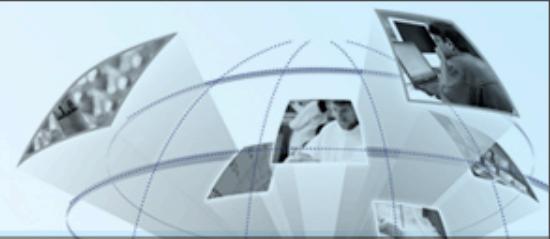
Ontologies
(structured
vocabularies) to
define relevant
properties



Our view of nanoinformatics



Our view of nanoinformatics



Overview of the NPO



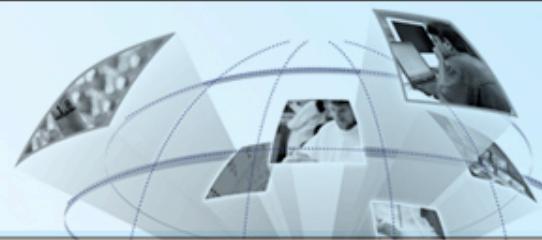
- Interoperability with existing resources

Overview of the NPO



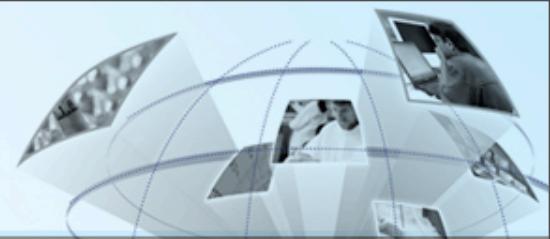
- Interoperability with existing resources
- Ontology Web Language format

Overview of the NPO

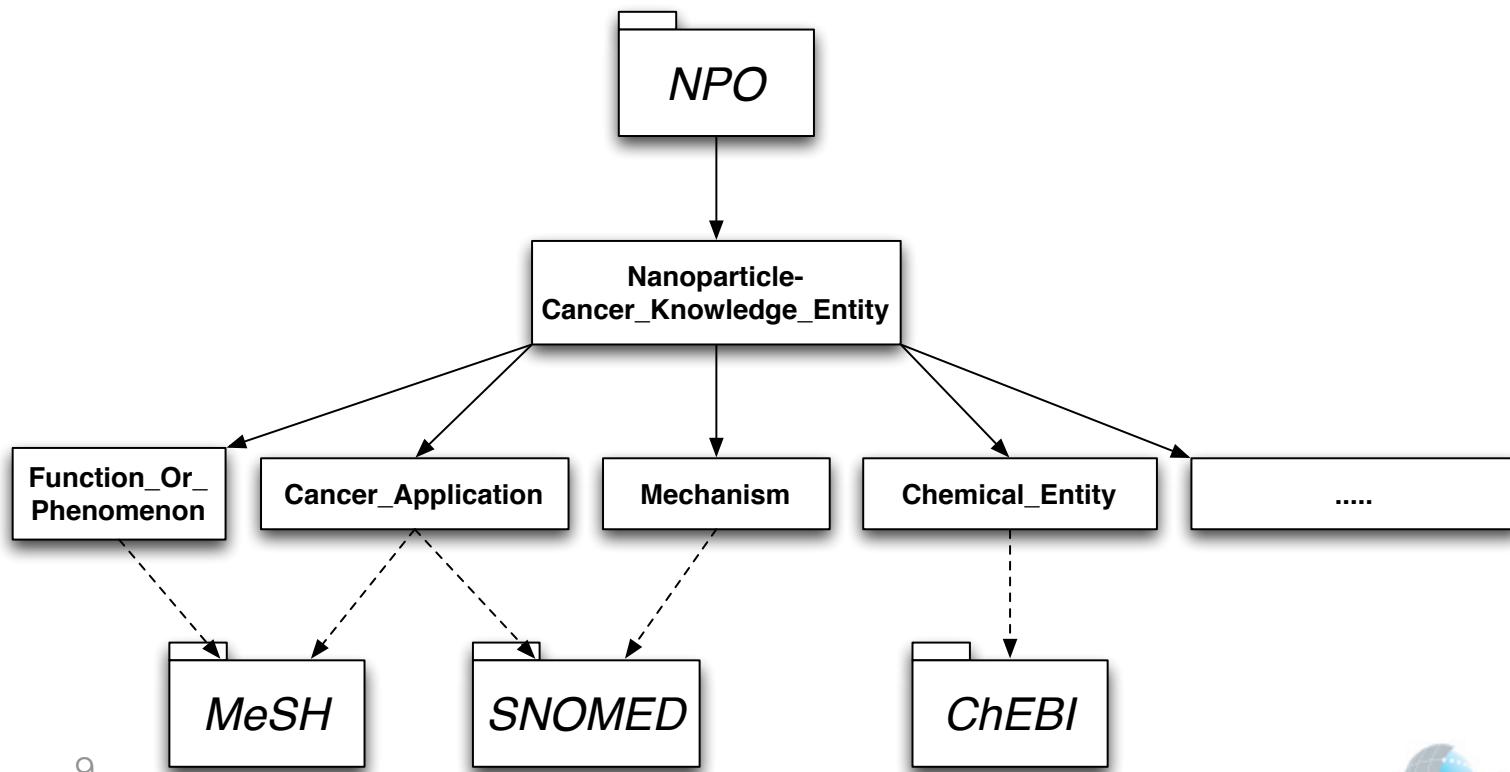


- Interoperability with existing resources
- Ontology Web Language format
- Protégé-based development

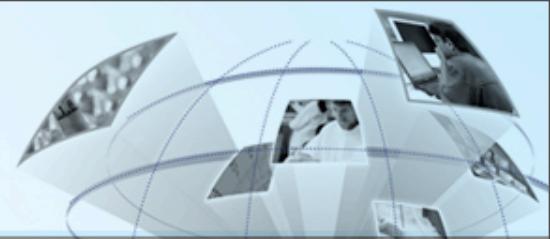
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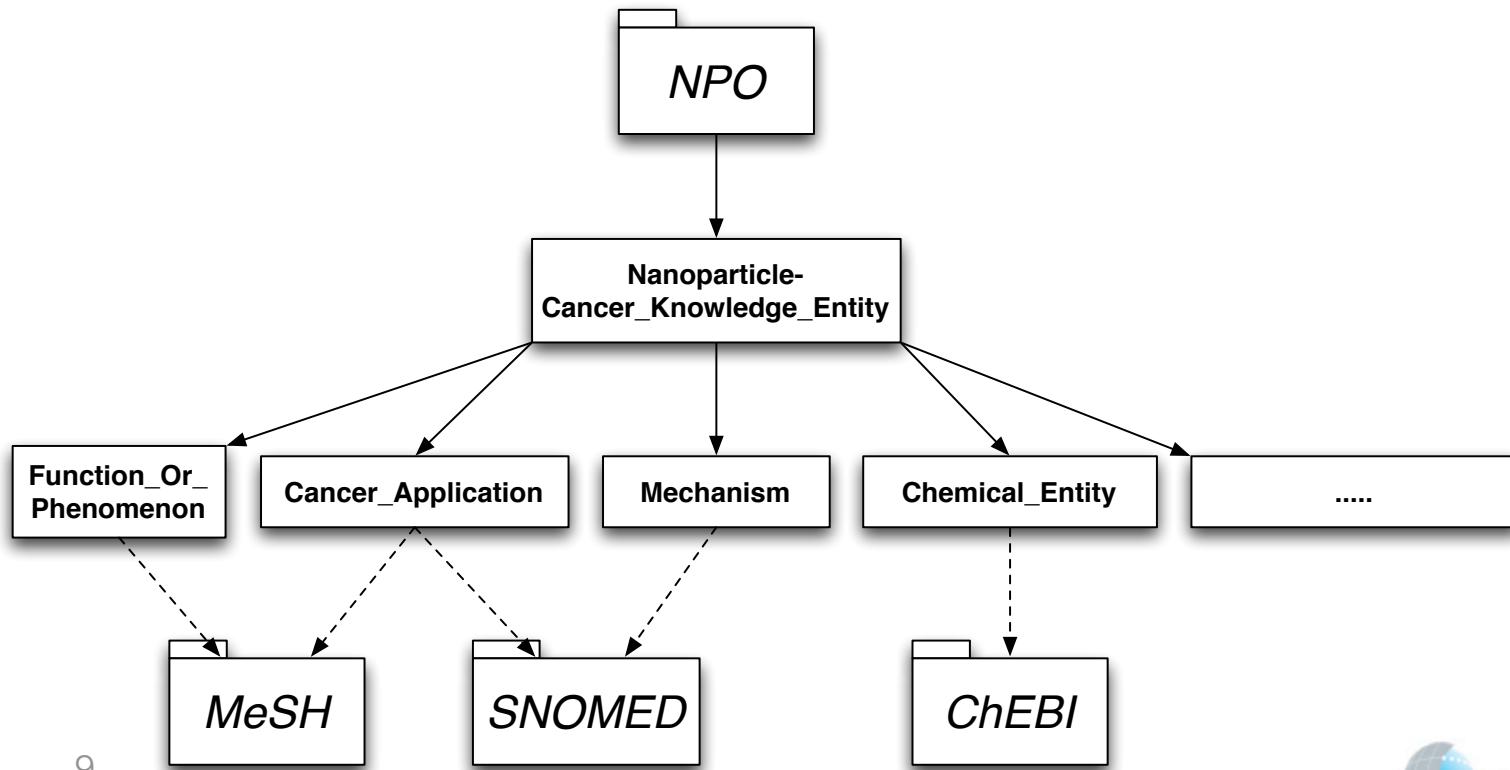
- Interoperability with existing resources
- Ontology Web Language format
- Protégé-based development
- Shared terminology with other vocabularies



Overview of the NPO



- Interoperability with existing resources
- Ontology Web Language format
- Protégé-based development
- Shared terminology with other vocabularies
- Under active development!



Example NPO classes



Example NPO classes



Top-level classes

- ▼ **Thing**
- **Extended_NPO**
- **Nanoparticle-Cancer_Knowledge_Entity**
 - **Cancer_Application**
 - **Chemical_Entity**
 - **Function_Or_Phenomenon**
 - **Mechanism**
 - **Nanoparticle_Composition_Descriptor**
 - **Nanoparticle_Experiment_Package**
 - **Nanoparticle_Formulation_Property**
 - **Nanoparticle_Interacting-Entity**
 - **Nanoparticle_Type**
 - **Stimulus_Description**

Example NPO classes



Top-level classes

- ▼ ● Thing
 - ● Extended_NPO
 - ● Nanoparticle-Cancer_Knowledge_Entity
 - ● Cancer_Application
 - ● Chemical_Entity
 - ● Function_Or_Phénoménon
 - ● Mechanism
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 - ● Nanoparticle_Experiment_Package
 - ● Nanoparticle_Formulation_Property
 - ● Nanoparticle_Interacting_Entity
 - ● Nanoparticle_Type
 - ● Stimulus_Description

Chemical composition class

- ▼ ● Nanoparticle_Chemical_Composition_Descriptor
 - ▼ ● Chemical_Component_In_Nanoparticle_Formulation
 - ▼ ● Chemical_Component_For_Nanoparticle_Functionality
 - Targeting_Chemical_Component
 - Chemical_Constituent_Of_Nanoparticle
 - Nanoparticle
 - ▼ ● Linkage_Descriptor
 - Linkage
 - ▼ ● Linkage_Chemical_Component
 - Attached_Chemical_Component
 - ▼ ● Entrapped_Chemical_Component
 - Encapsulated_Chemical_Component
 - ▼ ● Linkage_Interaction
 - ● Covalent_Interaction
 - ● Non-Covalent_Interaction
 - ▼ ● Linkage_Type
 - ▼ ● Attachment
 - Chemical_Conjugation
 - ▼ ● Entrapment
 - Encapsulation
 - Nanoparticle_Formulation

Example NPO classes



Top-level classes

- ▼ ● Thing
- ● Extended_NPO
- ▼ ● Nanoparticle-Cancer_Knowledge_Entity
 - ● Cancer_Application
 - ● Chemical_Entity
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 - ● Mechanism
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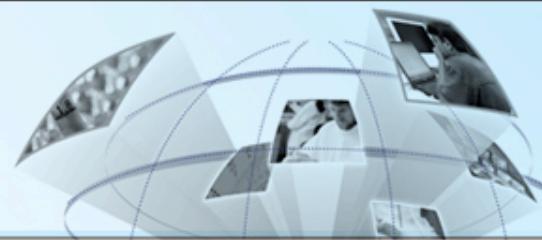
Chemical composition class

- ▼ ● Nanoparticle_Chemical_Composition_Descriptor
- ▼ ● Chemical_Component_In_Nanoparticle_Formulation
 - ▼ ● Chemical_Component_For_Nanoparticle_Functionality
 - Targeting_Chemical_Component
 - Chemical_Constituent_Of_Nanoparticle
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 - ● Covalent_Interaction
 - ● Non-Covalent_Interaction
 - ▼ ● Linkage_Type
 - ▼ ● Attachment
 - Chemical_Conjugation
 - ▼ ● Entrapment
 - Encapsulation
 - Nanoparticle_Formulation

Physical composition class

- ▼ ● Nanoparticle_Physical_Composition_Descriptor
- ▼ ● Nanoparticle_Physical_Site
 - ▼ ● Coat
 - Inner_Surface_Coat
 - Outer_Surface_Coat
- ▼ ● Nanoparticle_Boundary
 - Exterior_Surface_Of_Dendrimer
 - Outer_Hydrophilic_Surface_of_Liposome
 - Outer_Surface_Of_Nanotube
 - Surface
 - Surface_Of_Micelle
- ▼ ● Nanoparticle_Part
 - ▼ ● Core_Of_Nanoparticle
 - Dendrimer_Core
 - Hollow_Core_Of_Nanocage
 - Hollow_Core_Of_Nanocapsule
 - Hollow_Core_Of_Nanoshell
 - Nuclear_Core_Of_Nanocell
 - Dendrimer_Branch
 - Dendrimer_Cavity
 - Dendrimer_Generation_Layer
 - Hydrophilic_Core_Of_Liposome
 - Hydrophilic_Space_Between_Lipid_Bilayers
 - Hydrophobic_Core_Of_Lipid_Bilayer
 - Hydrophobic_Core_Of_Micelle
 - Nanopore
- ▼ ● Shell_Of_Nanoparticle
 - Nanocell_Membrane
 - Porous_Shell_Of_Nanocage
 - Shell_Of_Nanocapsule
 - Shell_Of_Nanoshell

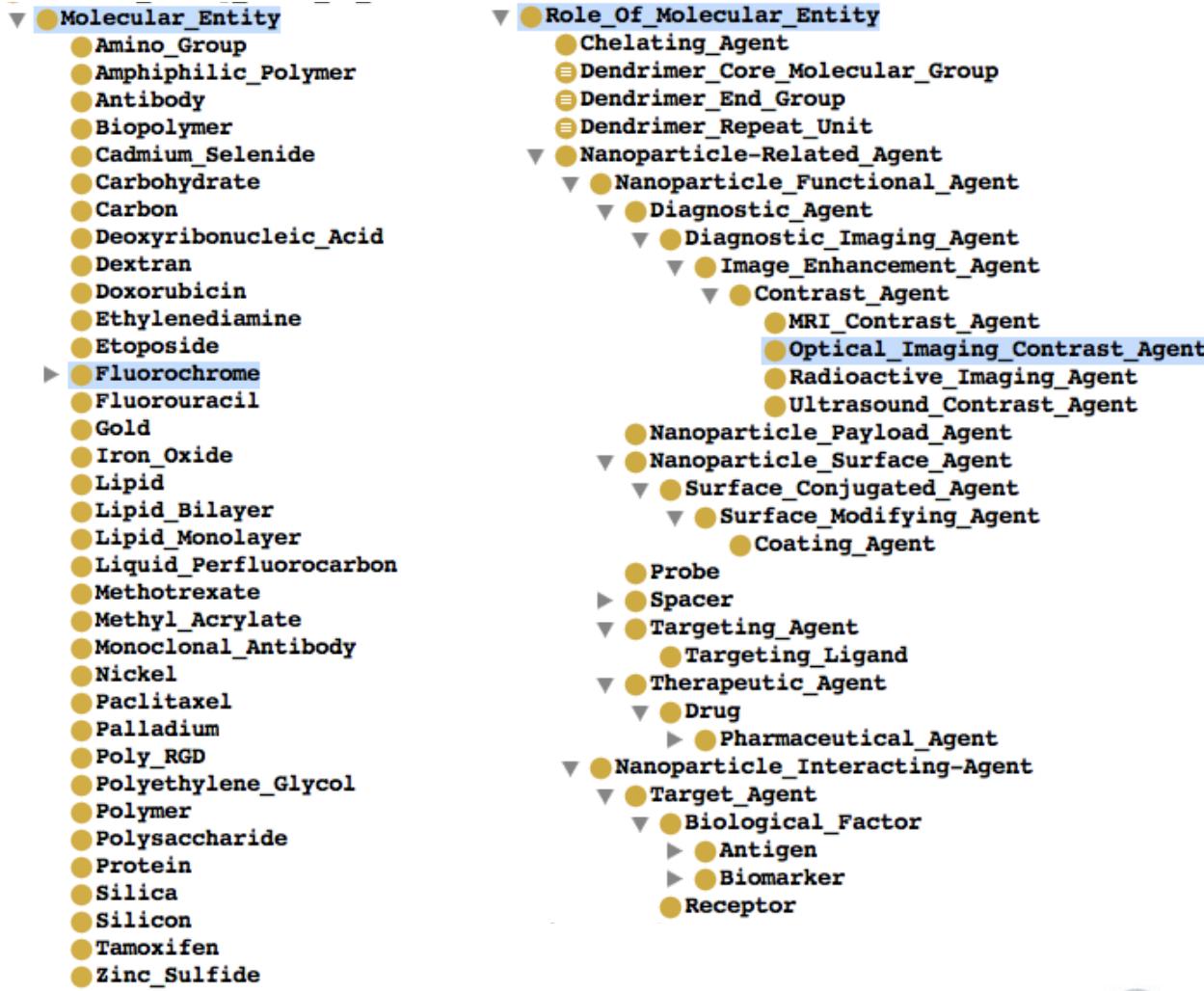
Example NPO classes



Example NPO classes



Molecular entity classes



Example NPO classes



Example NPO classes



Nanoparticle type classes

- ▼ ● Nanoparticle_Type
 - Antibody-Coated_Nanoparticle
 - Biopolymer-Coated_Nanoparticle
 - Carbohydrate-Coated_Nanoparticle
 - Core-Shell_Nanoparticle
 - DNA-Coated_Nanoparticle
- ▼ ● Dendrimer
 - Polyamidoamine_Dendrimer
 - Dextran-Coated_Nanoparticle
 - Doxorubicin-Loaded_Nanoparticle
 - Drug-Loaded_Nanoparticle
 - Etoposide-Loaded_Nanoparticle
- ▼ ● Fullerene
 - Buckybball
 - Gold-Dendrimer_Nanoparticle
 - Gold_Nanoparticle
 - Iron_Oxide_Nanoparticle
 - Lipid-Coated_Nanoparticle
- ▼ ● Liposome_Vesicle
 - Multilamellar_Vesicle
 - ▼ ■ Unilamellar_Vesicle
 - Large_Unilamellar_Vesicle
 - Small_Unilamellar_Vesicle
 - Methotrexate-Loaded_Nanoparticle
- ▼ ● Micelle
 - Polymer_Micelle
 - Monoclonal_Antibody-Coated_Nanoparticle
 - Nanoaggregate
 - Nanobud
- ▼ ● Nanocage
 - Gold_Nanocage
 - Nanocapsule
 - Nanocell
- ▼ ● Nanofiber
 - Carbon_Nanofiber
- ▼ ● Nanohorn
 - Single-Walled_Nanohorn
- ▼ ● Nanoparticle_Complex
 - Hybrid_Nanoparticle

- ▼ ● Nanoparticle_Function_Type
 - Nanoarray
 - Nanobomb
- ▼ ● Nanocantilever
 - Gold_Nanocantilever
 - Nanochannel
 - Nanoprobe
- ▼ ● Nanosensor
 - Fiber-Optic_Nanosensor
 - Nanopipette
- ▼ ● Nanorod
 - Multicomponent_Nanorod
 - ■ Bimetallic_Nanorod
- ▼ ● Nanoshell
 - Metallic_Nanoshell
 - Gold_Nanoshell
- ▼ ● Nanosphere
 - Silica_Nanosphere
- ▼ ● Nanotube
 - Carbon_Nanotube
 - Double-Walled_Carbon_Nanotube
 - Double-Walled_Nanotube
 - Multi-Walled_Carbon_Nanotube
 - Multi-Walled_Nanotube
 - Silicon_Nanotube
 - Single-Walled_Carbon_Nanotube
 - Single-Walled_Nanotube

- Nanowire
- PEG-Coated_Nanoparticle
- Paclitaxel-Loaded_Nanoparticle
- Palladium_Nanoparticle
- Perfluorocarbon_Nanoparticle
- Polymer-Coated_Nanoparticle
- Polysaccharide-Coated_Nanoparticle
- Protein-Coated_Nanoparticle
- ▼ ● Quantum_Dot
 - Cadmium_Selenide_Quantum_Dot
 - Gold_Quantum_Dot
 - Zinc_Sulfide_Quantum_Dot
- Silica-Coated_Nanoparticle
- Solid_Lipid_Nanoparticle
- Tamoxifen-Loaded_Nanoparticle

Example NPO classes



Nanoparticle type classes

- Nanoparticle_Type
 - Antibody-Coated_Nanoparticle
 - Biopolymer-Coated_Nanoparticle
 - Carbohydrate-Coated_Nanoparticle
 - Core-Shell_Nanoparticle
 - DNA-Coated_Nanoparticle
- Dendrimer
 - Polyamidoamine_Dendrimer
 - Dextran-Coated_Nanoparticle
 - Doxorubicin-Loaded_Nanoparticle
 - Drug-Loaded_Nanoparticle
 - Etoposide-Loaded_Nanoparticle
- Fullerene
 - Buckybball
 - Gold-Dendrimer_Nanoparticle
 - Gold_Nanoparticle
 - Iron_Oxide_Nanoparticle
 - Lipid-Coated_Nanoparticle
- Liposome_Vesicle
 - Multilamellar_Vesicle
 - Unilamellar_Vesicle
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 - Single-Walled_Carbon_Nanotube
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- Paclitaxel-Loaded_Nanoparticle
- Palladium_Nanoparticle
- Perfluorocarbon_Nanoparticle
- Polymer-Coated_Nanoparticle
- Polysaccharide-Coated_Nanoparticle
- Protein-Coated_Nanoparticle
- Quantum_Dot
 - Cadmium_Selenide_Quantum_Dot
 - Gold_Quantum_Dot
 - Zinc_Sulfide_Quantum_Dot
- Silica-Coated_Nanoparticle
- Solid_Lipid_Nanoparticle
- Tamoxifen-Loaded_Nanoparticle

Class Description: Gold_Nanoparticle

Equivalent classes +

- Nanoparticle_Type and has_Component some Gold and has_Component only Gold

Class Description: Tamoxifen-Loaded_Nanoparticle

Equivalent classes +

- Nanoparticle_Type and has_Component some (Nanoparticle_Payload_Agent and Tamoxifen)

Class Description: Antibody-Coated_Nanoparticle

Equivalent classes +

- Nanoparticle_Type and has_Component some (Antibody and Coating_Agent)

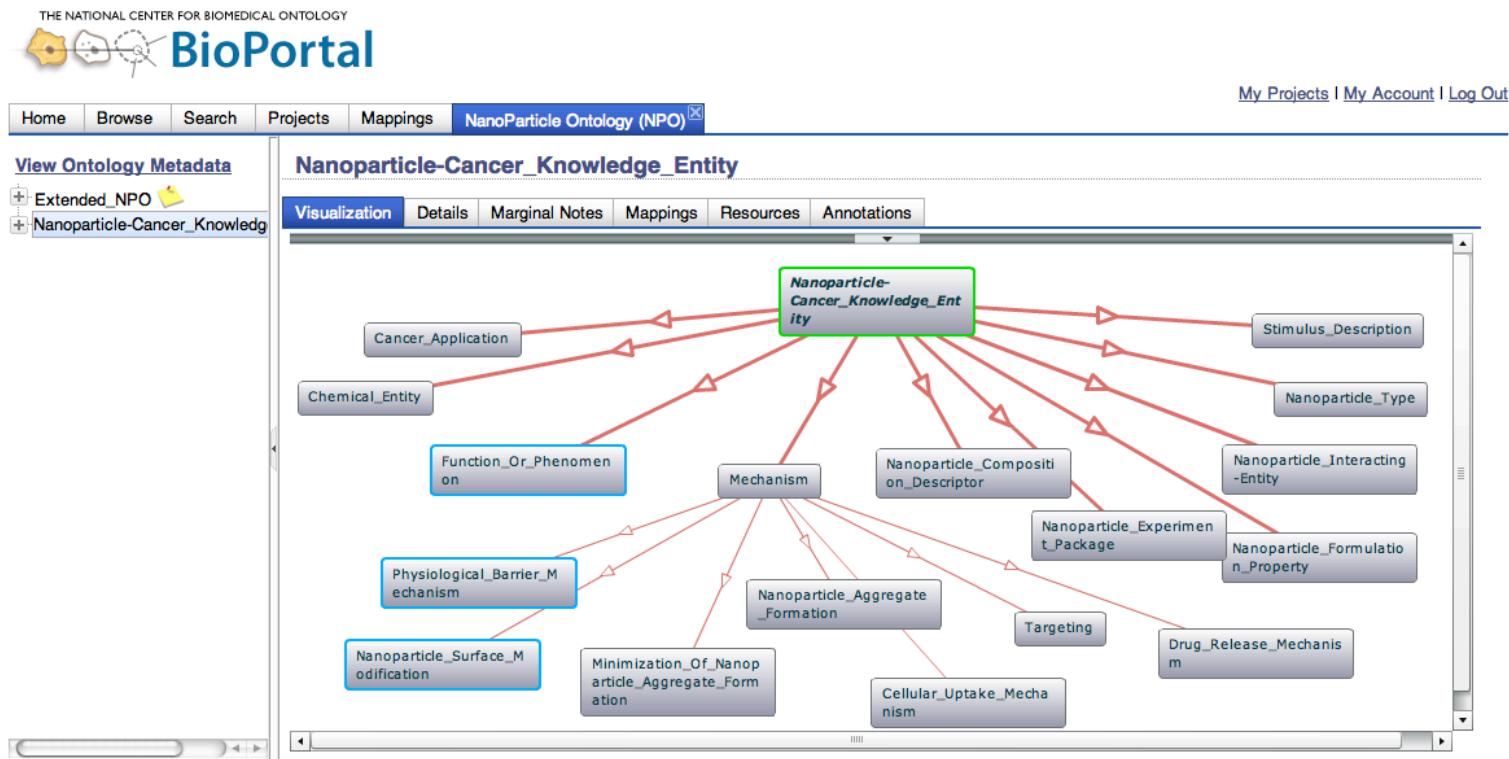
Availability of the NPO



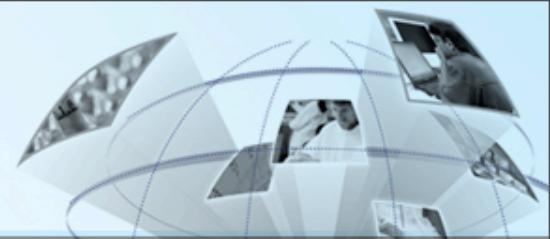
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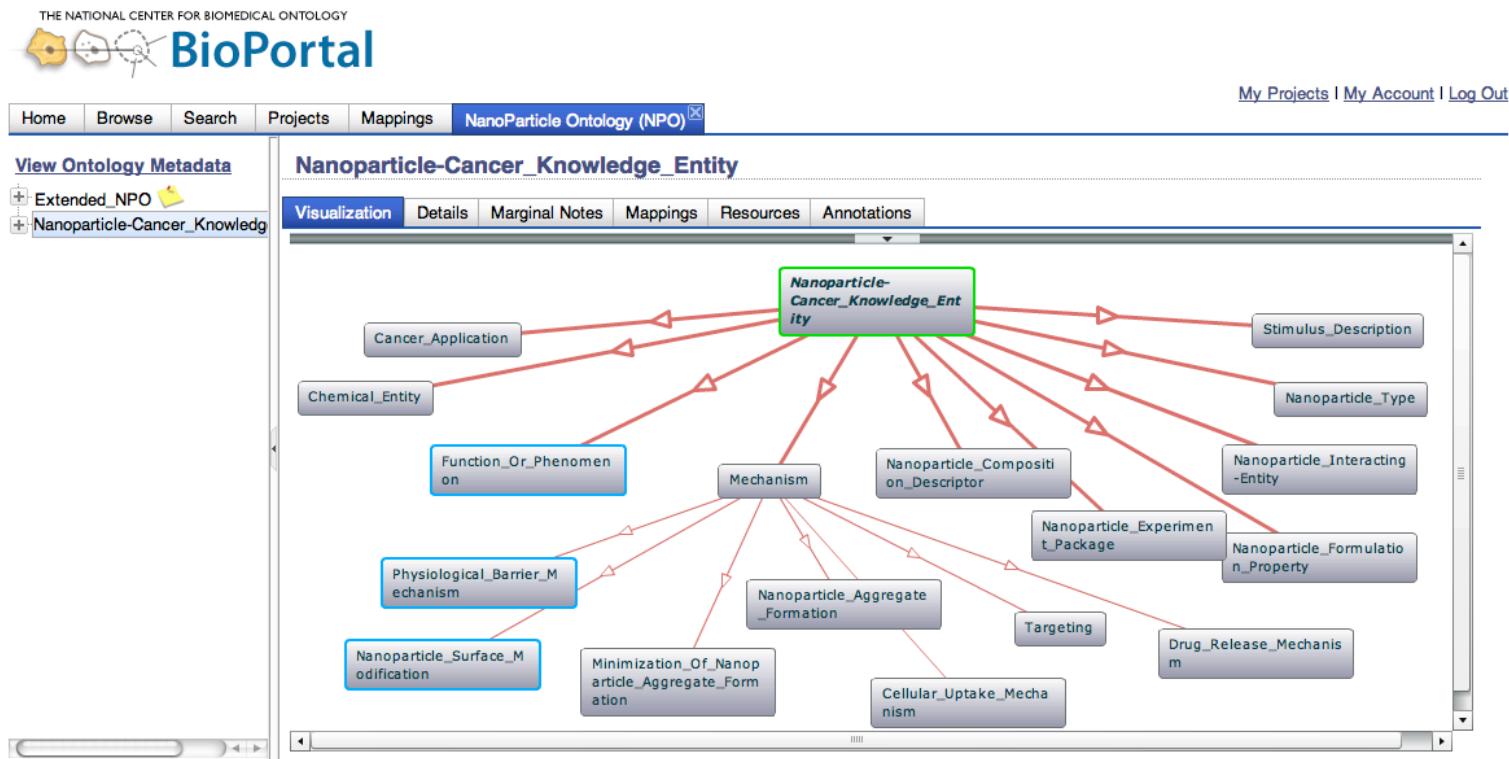
- Bioportal: <http://www.bioontology.org/tools/portal/bioportal.html>



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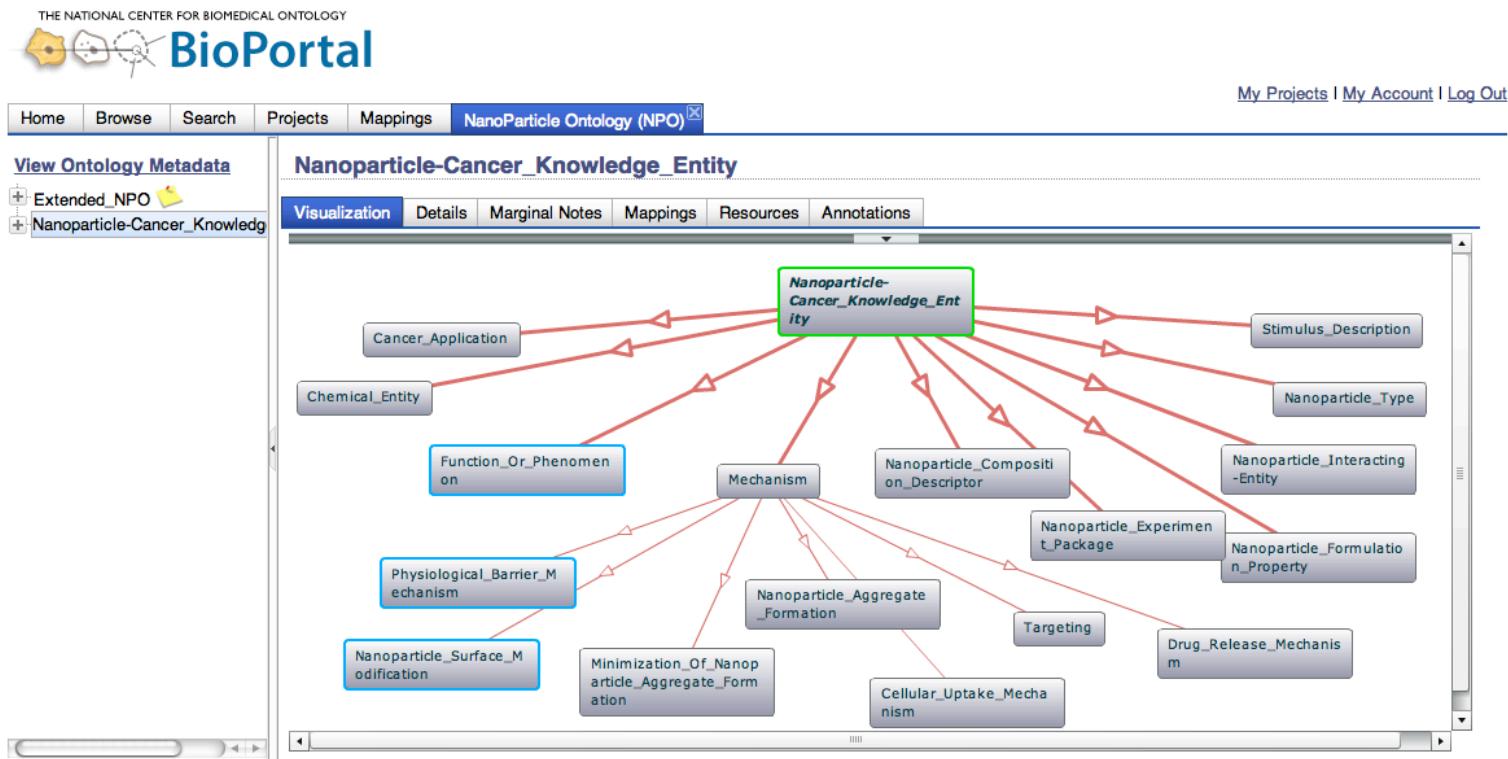
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- BiomedGT SMW: <http://biomedgt.org/> (NPO coming soon!)



Availability of the NPO



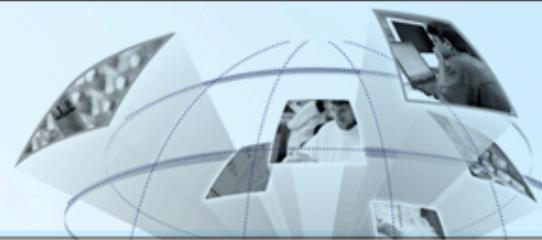
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Future vocabulary development



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- **Harmonization**
 - EVS terminologies
 - ChEBI
 - Other ontologies

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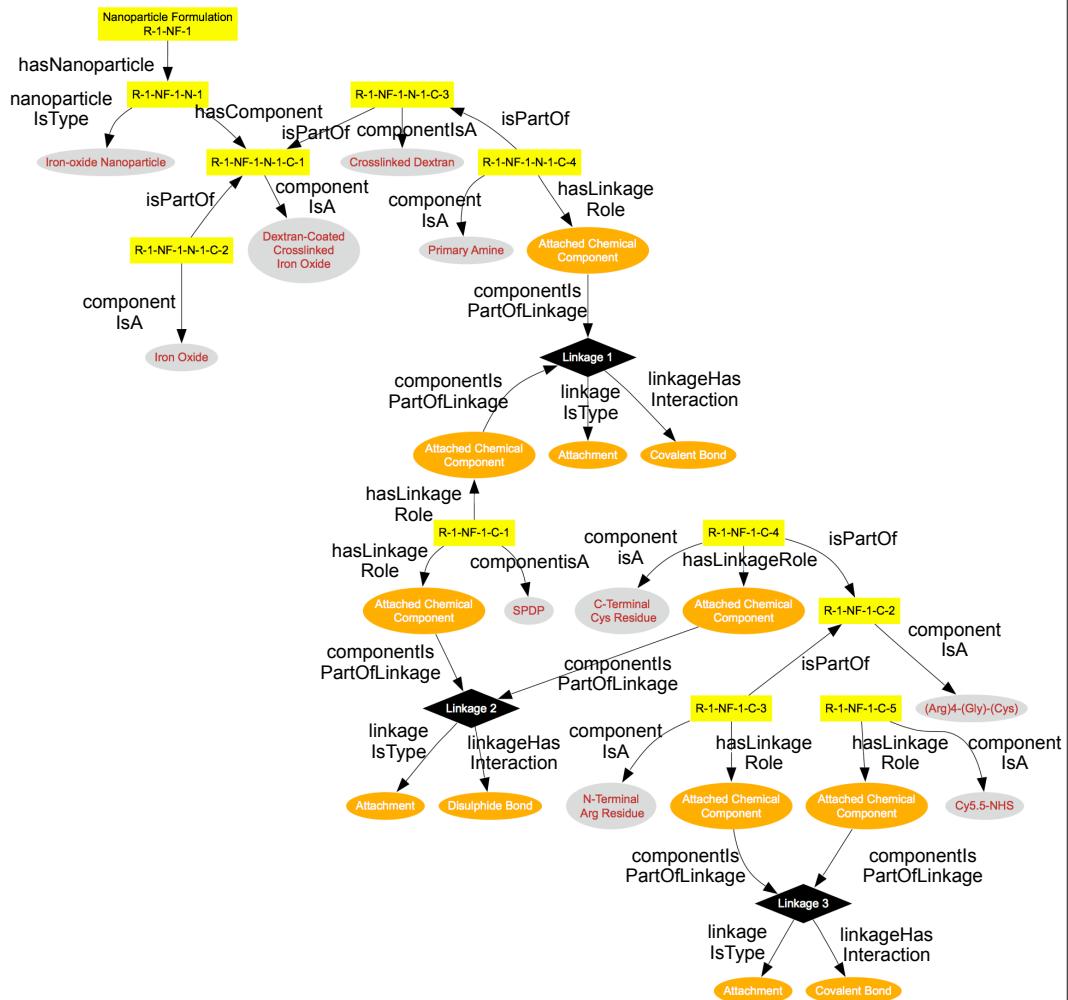


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- **Harmonization**
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 - **Application and integration:**
 - caNanoLab concepts
 - Other caBIG tools and infrastructure
 - Data annotation models



Acknowledgements



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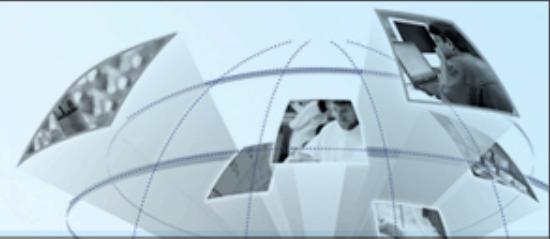


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Please visit the poster “Ontology and Object Model for Annotating Nanoparticles in Cancer Research” by Thomas DG, et al for more information!

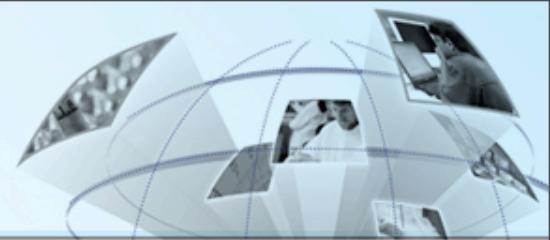


Other NPO 0.9.3 facts



- Total number of classes in the NPO = 496
- Total number of relations at the class-level = 32
- The NPO contains terms that can be used for classifying nanoparticles, formulated for diagnostic/therapeutic purposes, based on their
 - Structure and role of chemical components
 - Spatial arrangements of the chemical components
 - Structure, shape and function of the nanoparticles,
 - Underlying mechanism guiding the design of nanoparticles
 - Intended application of the nanoparticles
 - Functions or processes in which a nanoparticle participates or has a role in
 - Function-specific properties of the chemical components associated with a nanoparticle
 - Physical state in which the nanoparticles are formulated
 - Stimulus for triggering the functionality of a nanoparticle
- The NPO also includes terms that are part of the annotation model, which provides a structural framework for annotating nanoparticle data using the above classification scheme
- The NPO also contains terms of another annotation model developed for providing the structural framework for annotating preparation/synthesis steps of a nanoparticle formulation

Additional NPO 0.9.3 facts



1. The NPO provides a common vocabulary of terms for annotating nanoparticles based on our classification scheme
2. The NPO contains only limited number of terms, and hence, one will not find terms for annotating all nanoparticles that exist in the literature
3. The NPO lacks a formal structure and sometimes a term's ontological description is not fully explicit, due to which 1) the NPO is not readily interoperable with other existing ontologies, 2) it makes it difficult for manually navigating the ontology and for adding terms by multiple ontology developers.
4. To solve the problems noted in point #3, we plan to divide the NPO into
 - a. a reference ontology that contain terms used for annotating data, and
 - b. an information ontology containing terms of the annotation models , which will help one to guide the annotation of nanoparticle data using terms from the reference ontology